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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,745	04/06/2006	Suraj Shivappa Shetty	PC/4-33421A	2533

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ONE HEALTH PLAZA 104/3
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EXAMINER	
JEAN-LOUIS, SAMIRA JM	
ART UNIT	PAPER NUMBER
1627	

MAIL DATE	DELIVERY MODE
11/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,745	SHETTY ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *3-5,9-12 and 14-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-8 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/19/09*.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application.

6)☐ Other: _____.

DETAILED ACTION

Response to Arguments

This Office Action is in response to the amendment submitted on 08/28/09. Claims 1-17 are currently pending in the application, with claims 3-5, 9-12, and 14-17 having being withdrawn. Accordingly, claims 1-2, 6-8, and 13 are being examined on the merits herein.

Receipt of Applicant's remarks and IDS is acknowledged and has been entered.

Applicant's argument that while Brater teaches bumetanide as 40-50 times as potent, Brater teaches that the time at which peak urinary excretion rate of the drug revealed negligible differences between bumetanide and furosemide at the doses used in their study has been fully considered. Consequently, Applicant contends that in light of the teachings of Brater, one of ordinary skill would not be motivated to add the bumetanide of Brater since even the enhanced potency of bumetanide still provided no improvement in the peak urinary excretion rate for bumetanide as compared to furosemide. Moreover, applicant argues that oral dosing could not be discerned further supporting the notion that one of ordinary skill in the art would not have added bumetanide to the composition of Alexander. Such arguments are not found persuasive as Alexander explicitly teaches the use of an ALDO such as eplerenone, ARB such as valsartan, and a diuretic agent in combination. Alexander however does not teach addition of bumetanide to the composition of Alexander. Brater, on the other hand,

does teach that bumetanide is 40-50 more potent than common diuretics such as furosemide. Brater, also teaches that bumetanide possesses prolonged absorption in congestive heart failure patients (CHF) as compared to normal subjects. While applicant argues that no improvement in peak urinary excretion rate was observed as compared to furosemide (i.e. time course of absorption), the Examiner maintains that one of ordinary skill in the art would have indeed found it obvious to add bumetanide to the composition of Alexander since Brater teaches that bumetanide has high potency properties and that administration of bumetanide to CHF patients resulted in increased and prolonged absorption (see abstract). Moreover, Brater teaches that bumetanide had an 80% bioavailability as compared to furosemide. Consequently, if one of ordinary skill desired increased bioavailability and enhanced potency of a diuretic, one of ordinary skill in the art would have indeed found it obvious to add bumetanide to the composition of Alexander with a reasonable expectation of providing a composition that is effective as a diuretic and a composition with enhanced bioavailability of the diuretic. Thus, the Examiner maintains that Alexander in view of Brater does indeed render obvious applicant's invention.

For the foregoing reasons, the rejection of record under 103 (a) remains proper and is maintained. It is being made Final and is re-stated below for applicant's convenience.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 6-8, and 13 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Alexander et al. (U.S. 6,653,306 B1, previously cited) in view of Brater et al. (Kidney International, 1984, Vol. 26, pgs. 183-189, previously cited).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Alexander et al. teach a combination comprising therapeutically-effective amount of an epoxy-steroidal aldosterone receptor (ALDO) antagonist and a therapeutically-

effective amount of an angiotensin II receptor antagonist (ARB) for the treatment of circulatory disorders including cardiovascular disorders such as hypertension, congestive heart failure (CHF), cardiac hypertrophy, cirrhosis and ascites (see abstract, col. 1, lines 10-20, and col. 4, lines 26-33). Alexander et al. also teach that by combination therapy, it is meant that the ARB and the ALDO combined preparation entails administration of the compounds in a sequential manner (instant claim 13) or in a simultaneous manner in a single capsule or in multiple separate capsules for each antagonist (see col. 4, lines 61-67 and col. 5, lines 1-2). Particularly, Alexander et al. teach that the combination therapy can consist essentially of an ARB, an ALDO, and a diuretic (instant claims 1 and 6-7; see col. 5, lines 10-12 and col. 14, lines 18-26). Preferred ALDO include eplerenone (instant claims 2 and 8; see col.5, table 1). Preferred ARB include valsartan that can be combined with the ALDO (instant claims 2 and 8; see col. 281, claims 17-19).

Alexander et al. however does not specifically teach addition of bumetanide as the diuretic in the composition.

Brater et al. teach the use of bumetanide in congestive heart failure patients (see abstract). Particularly, Brater et al. teach bumetanide is a new loop diuretic which is 40 to 50 times as potent as furosemide, an older diuretic with a twofold shorter elimination half-life (see pg. 183, left col., last paragraph and pg. 188, left col., lines 3-4). Importantly, Brater et al. teach that bumetanide has a two-fold greater bioavailability as

compared to the older diuretic furosemide in normal and congestive heart failure patients though a delayed rate of absorption was observed in congestive heart failure patients (see pg. 183, left col., last paragraph, pg. 187, right col., top paragraph, and pg. 188, left col., lines 18-22).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to add the bumetanide of Brater et al. into the combined composition of Alexander et al. since Brater et al. teach that bumetanide is 40-50 more potent and more bioavailable than older diuretics. Moreover, at the time of Applicant's invention, it would have been obvious to one of ordinary skill in the art to include a label and packaging in the combined composition of Alexander and Brater et al. One of ordinary skill in the art would have been motivated to include the packaging and the insert, because it is mandated by law.

Further, it is well-settled law that combining printed instructions and an old product into a kit will not render the claimed invention non-obvious even if the instructions detail a new use for the product. *See In re Negai, 367 F.3d 1336, 1339, 70 USPQ2d 1862, 1862 (Fed. Cir. 2004*). Further, the inclusion of a package insert or label showing "the name of drug, dosage form, route of administration, indication and direction of use" of a pharmaceutical composition is mandated by 21 CFR 201.57 and is therefore obvious to one of ordinary skill in the art.

Thus, given the teachings of Alexander and Brater, one of ordinary skill would have been motivated to add bumetanide into the combined preparation/kit of Alexander et al. with the reasonable expectation of providing a combination that is effective in treating circulatory disorders including congestive heart failure and a combination that is highly bioavailable.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1627

11/21/2009

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627